comprising a sequence segment complementary to a nucleic acid sequence of interest, or complementary to a nucleic acid sequence of interest except at a position of interest or probed position which comprises the position pairing to a degenerately pairing nucleotide. Additional probes or hybridizing nucleotide sequences are required if there are more than four nucleotides that may be present at the variable position or position of interest. For four possible nucleotides in a sequence, two nucleic acid hybridizing sequences are required each having a nucleotide base pairing to a set of two nucleotides at the variable position, the two sets overlapping in one nucleotide, which is common to both sets.

Please amend the specification at page 16, line 15, through page 17, line 2, as indicated in Appendix A. The amended portion of the specification will then read as follows:

The term "hybridization probe" as used herein refers to a nucleic acid sequence that by itself or as a member of a set of nucleic acid sequences or probes for a specific nucleic acid sequence, effects the hybridization of a specific target sequence. The hybridization probes of the invention comprise a nucleic acid sequence segment having sequence complementary to the analyte sequence of interest. Such probes may comprise nucleic acid sequence for potential hybridization with analyte only, or may additionally comprise a discrete tagging or labeling moiety, such as a chemiluminescent moiety or a discrete nucleic acid sequence that is not a putative anti-target or anti-analyte sequence, but functions solely to indicate the presence of the probe. Such hybridization probes include sequences that form hybrids for enzymatic amplification such as primers for polymerase chain reaction amplification and sequences forming double stranded complex replication templates for enzymes such as the RNA replicases. In addition to hybridizing probes for an amplification process, probes for simple hybridization and detection, both tagged or labeled with a discrete moiety and not labeled with any discrete label moiety are contemplated. Nucleic acid sequences comprising probes not having a discrete labeling moiety may be intrinsically labeled for detection of the hybridization, as by incorporation of ^{32}P into the nucleic acid phosphodiester backbone or the like. Hybridization probes may comprise a sequence complementary to the sequence to be detected and detectable signal or marker indicating the presence of the complementary sequence, for example a separate moiety such as a chemiluminescent marker, or ^{32}P incorporated into the phosphodiester backbone of the nucleic acid sequence or both.

Please amend the specification at page 18, line 32, through page 19, line 13, as indicated in Appendix A. The amended portion of the specification will then read as follows:

The sequence is deduced by reassembly of the sequence of known (N-1)-mer overlapping oligonucleotides that hybridize to the target nucleic acid to generate the sequence of the target nucleic acid, which cannot be accomplished in some cases because some information is lost if the target nucleic acid is not in fragments of appropriate length in relation to the size of the oligonucleotides that are used for the hybridization probes. The quantity of information lost is proportional to the length of a target being sequenced. However, if sufficiently short targets are employed, their sequence can be unambiguously determined. The deductive construction of the sequence is interrupted in analyte sequence regions where a given overlapping (N-1)-mer is duplicated to appear at least three times in succession, e.g. repeated two or more times, causing the deduced sequence to skip the second and subsequent repetitions in sequence. At such points either of two different N-mers, differing in the last nucleotide are deduced for extending the sequence construction. Such branching points of sequence deduction limit unambiguous assembly of a sequence.

Please amend the specification at page 20, lines 23-33, as indicated in Appendix A. The amended portion of the specification will then read as follows:

Another sequencing method that relies upon hybridization employs a label or tag that identifies the specific hybridizing sequence. For example a different fluorescent marker can be linked to each possible sequence of three nucleotides (4^3 or 64 in all), and a sequence may be obtained by successive hybridization and digestion of three nucleotides at a time. The sequence may also be obtained by labels comprising a nucleotide sequence, for example the start codon AUG may be labeled by the sequence 5'-AAAAAAAAACCCCCTTTTCTTTT (SEQ ID NO: 11), which will form a hairpin loop self complementary structure that can be differentiated from like labeling structures, such as 5'-AAAAAAAAACCCCCTTTTTTTTT (SEQ ID NO: 12) and 5'-AAAAGAAAACCCCCTTTTCTTTT (SEQ ID NO: 13), by the temperature that causes a loss of such secondary structure.

Please amend the specification at page 22, line 23, through page 23, line 29, as indicated in Appendix A. The amended portion of the specification will then read as follows:

The nucleic acid analog 8-oxo-dGTP (Amersham, Cambridge UK) is formed spontaneously by oxidation of dGTP in the context of normal cellular metabolic activity. 8-oxo-dGTP has one form which can behave as either dG to pair with C (FIG. 2) in a standard base pairing steric arrangement or as dT to pair with A (FIG. 3) in a sterically atypical base pairing arrangement resembling a wobble base pairing arrangement. Thus 8-oxo-dG at a position in a nucleic acid sequence pairs with both C (as dG) and A (as dT) in close amounts indicative of moderately different binding energies. Thus 8-oxo-dG may be incorporated in a nucleic acid sequence for either G or T almost equally in a proportion relative to the total number of G or T in the polymerization mixture. When replicated a position incorporating 8-oxo-dG is polymerized as the complementary sequence to the template having 8-oxo-dG incorporated at the position of interest as a G, therefore causing only dC to be incorporated at that incoming nucleotide position because of the difference in free energies between the two base pairing interactions, e.g. 8-oxo-dG::C versus 8-oxo-dG::A. FIG 2 shows that 8-oxo-dG::C has three H bonding interactions compared to two for 8-oxo-dG::A (FIG. 3), which is not a standard Watson-Crick base pairing interaction. Because in a polymerase reaction mixture containing all the nucleotides plus 8-oxo-dG, a proportion of sequence positions having a T (pairing A) are substituted with 8-oxo-dG, which then pairs with C, the purine A is effectively converted to the pyrimidine C, and T is converted to G. Such random or stochastic transmutation is from purine to pyrimidine and visa versa, a transmutation termed transversion. Note that dGTP could be absent from the polymerase mixture and wholly replaced by 8-oxo-dG, but this will not typically be the case. Because dTTP and 8-oxo-dGTP are necessarily present in the reaction mixture, the replacement of T with 8-oxo-dG will be proportionate to the relative amounts, and therefore concentrations of the two dNTPs. For replication, the presence of the 8-oxo-dG causes the incoming nucleotide for the complementary nascent strand synthesized from the 8-oxo-dG containing template to be dC exclusively, and the dC then causes a dG to be inserted for subsequent polymerization using the new strand as a template. Thus, the 8-oxo-dG in a sequence behaves as a G for the purpose of synthesis from a template containing the 8-oxo-dG. If all four standard dNTPs (A,T,C,G) are present in the polymerization mixture along with 8-oxo-dG, then the sequence having random substitution of 8-oxo-dG for T forms a template for further polymerization in which the complementary substitution of A for C occurs along with the complementary substitution of T for G. Such mutations from purine to pyrimidine and visa versa are known as transversion mutations. Thus although mechanistically somewhat different than the random mutagenesis effected via dPTP, while still depending upon degenerate base pairing, 8-